

Appln No.: 09/937,192

Amendment Dated: December 27, 2004

Reply to Office Action of June 25, 2004

REMARKS/ARGUMENTS

This is in response to the Office Action mailed June 25, 2004 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants request a three month extension of time for response and enclose a Credit Card form for the payment of the fee. The Commissioner is authorized to charge any additional fees or credit any overpayment to Deposit Account No. 15-0610.

The Examiner has reopened prosecution following an Appeals Conference, and now presents two rejections under 35 USC § 112, first paragraph. The first of these rejections is for lack of written description, the second for lack of enablement. Applicants respectfully traverse both of these rejections.

With respect to the written description rejection, the Examiner first asserts that the

independent claims require "a chemical compound comprising first and second hsp-binding moieties which bind to the pocket of hsp90 to which ansamycin antibiotics bind, said binding moieties being connected to one another by a linker." The claims do not require that the compound possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity.

Applicants have amended the independent claims to make it clear that the hsp-binding moieties retain the ability to bind to hsp90 after they are incorporated in the compound. The independent claims have also been amended to specify that the binding moieties are ones that lead to degradation in proteasomes of a subset of proteins requiring hsp90 for conformational maturation, and that this activity is also retained in the compositions of the invention. This amendment is supported on Page 2, lines 1-2.

It is believed that this amendment overcomes the rejection for lack of written description. The claims now specify a biological activity and the maintenance of this activity when the composition of the invention is formed. The list of things that can be chemical compounds that spans Pages 2 and 3 of the office action has no connection to the claim as now presented, when read in light of the specification, and is merely a meaningless laundry list in the absence of any suggestion by the Examiner of compounds from this list that might actually meet the requirements of the claims of binding within the hsp90 binding pocket to result in protein degradation when combined in a homo or heterodimer as described in this application.

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What this application describes and claims is the discovery that if a compound binds to the designated hsp90 pocket and leads to protein degradation that the "dimer" form of that compound is also desirable. This is Applicants' invention, and it is supported by an adequate written description.

The Examiner's remarks concerning this rejection are really only the ultimate conclusion of a lack of written description. As such, it is Applicants' position that the Examiner has failed to meet the burden of "presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. MPEP § 2163 (II)(a). Based on the statement of the scope of the claims in the Official Action, he has failed to correctly determine what the claims as a whole covers. Further, he has not alleged any inadequacy in the number of disclosed species within the claimed genus, although he also has not acknowledged the number of species that are disclosed. Accordingly, Applicants submit that the Examiner has failed to put forward "evidence or reasons" supporting the rejection, and that it therefore should be withdrawn. Should the Examiner wish to maintain the rejection, then Applicants submit that it is the Examiner's obligation to show how the facts of the multitude of cases cited relate to this application.

The Examiner also rejected claims 3, 4, 6 and 9-34 under 35 USC for lack of enablement, stating that the claims are only enabled for the a compound in which both chemical moieties are geldanamycin, the linker is a 4 carbon linker bonded to the 17-carbon of geldanamycin, and to the use of this compound in the treatment of breast cancer.

The Examiner has not provided a single concrete example of a compound that based on a reasoned assessment might be expected to bind to the hsp90 binding pocket or offered any reason why the synthesis of a linked dimer compound based on such a starting material would require undue experimentation. The type of chemistry that is involved in the attachment of the linker is purely routine.

Furthermore, the Examiner's limiting the scope of enablement to compounds with 4 carbon linkers is inconsistent with the specification. The specification discloses results from compounds with two geldanamycin moieties linked by 4, 7, 9, and 12 carbon linkers. In each case, activity and selectivity is observed, although the 4-C linker was most active and most selective. (see Table 1). Further, the specification discloses other forms for linkers, including the aryl linker and the N-methyl-amino linker shown in Fig. 1. The specification also lists another species of ansamycin antibiotics, herbimycin (Page 1, line 26) and references WO98/51702 which refers to other hsp90 binding moieties such as macbecin, another ansamycin antibiotic. Thus, the disclosure is not limited to geldanamycin homodimer, and in fact provides (in example 1, Page 9, lines 15-23) a procedure for making a geldanamycin-herbimycin heterodimer.

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As to the statement that the claims are only enabled for breast cancer, the Examiner has not provided a single argument addressed to this point. He has cited cases, including the *Amgen* case which relates to written description not enablement (Page 10), and references a case that refers to "probable utility" but has not applied any of this to the present matter. Thus, he has failed to meet the burden placed on the Examiner in making an enablement rejection of providing acceptable reasoning inconsistent with enablement. *In re Strahilevitz*, 212 U.S.P.Q. 561, 563 (C.C.P.A. 1982). Further, to the extent the Examiner is asserting that the claimed invention may not work in cancers other than breast cancer, the Examiner is required to support an enablement rejection where the operability of materials beyond the scope of specific examples is challenged by the Examiner. *In re Bowen*, 492 F. 2d 859, 181 U.S.P.Q. 48 (C.C.P.A. 1974). This has not been done. Thus, the Examiner has failed to present an enablement rejection to which Applicants can reasonably respond. The rejection should therefore be withdrawn.

It is also noted that the Examiner has, despite repeated requests by Applicants, once again not even mentioned the declarations and the exhibits A-H which are of record in this case. The Examiner cannot pick and choose among the evidence of record, but must consider all of the evidence. Accordingly, should the rejection of the present claims be maintained, Applicants DEMAND a statement by the Examiner that these materials have been considered and an explanation as to why the Examiner finds them insufficient.

Finally, the Examiner has provisionally rejected the claims of this application for § 101-type double patenting in view US 09/937,192. Applicants note this rejection. However, the present claims were not before and are not now identical. Accordingly, this rejection should be withdrawn.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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